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EDITORIAL

It is so well known that anæsthetists, at any rate up till recently, have been the very incarnation of modesty, invariably deferring to the wishes of the surgeon, except in cases of extreme urgency and importance, that it is unnecessary to call attention to the matter. Nevertheless it is possible to wonder if this characteristic is not carried to extremes when one sits on the Appointments Committee of a Regional Hospital Board as a university representative or external assessor.

Not long ago an experience of one of us gave rise to these questionings. Half a dozen candidates applied for the post of maximum session part-time anæsthetist at a comparatively small hospital. Three of them turned up for interview, viz. a general practitioner (a local man), an S.H.M.O., and a consultant anæsthetist. The general practitioner got the post. The university representative and the external assessor, in deference (a case of habit, perhaps) to the wishes of the local representatives, agreed to the appointment, but asked the Chairman to make a record that they did this only in deference to the wishes of the local surgeons as both the status and the experience of the consultant far outweighed those of the general practitioner. Had the case come before

a neutral tribunal there is no doubt that the consultant would have obtained the post. Is this right? If not, what is the remedy? If it is, what is the function of the university representative or the external assessor? In spite of all the evidence to the contrary it is by no means certain that the decision was wrong. The hospital concerned was small, there would have been little scope for the skill and experience of the consultant, and it is possible that his new colleagues might not have given him as hearty a welcome as he would have liked.

The consultant was obviously a man of ability with a strong sense of humour, and made an excellent impression on the Board. Unless rapid and unforeseen developments in the surgery of the hospital were about to take place it was difficult to see what satisfaction he would have got out of the appointment. Are we as a Board to be congratulated on allowing the imponderables of the situation to outweigh the evidence?

It is probable that it is desirable to have a university representative and an external assessor on these Boards; even if they appear to play a subsidiary role, they may prevent gross abuse.

In this number we are publishing two articles sent to us from the United States on the history of the Rotameter. We do not feel it necessary to apologize for the inclusion of two articles on the same subject inasmuch as they are complementary to each other, and in view of the interest in this subject which has arisen as a result of the correspondence in past issues.

We are continuing to feature cases taken from the Morbidity Conference and would ask once again those

responsible for these Conferences to consider sending us suitable cases.

With great respect we would draw the attention of all our contributors to the Notice on the inside of the front cover of the Journal. It is true to say that in 90 per cent of cases the references to the papers submitted have to be redrafted by the Editorial Staff and retyped. In some instances where references are copious this rearranging may entail also retyping of the whole paper. For each issue of the Journal this implies a great deal of work. There is no doubt that we are not the only Journal which has these difficulties, and we hope it will not be taken amiss if once again we ask authors intending to submit contributions to any medical journal to make themselves acquainted with the conventions in regard to lay-out and references which are followed by the publication they intend to favour.

DOES ETHER AFFECT THE EXTENSIBILITY OR ELASTIC RECOIL OF MUSCLE?

By J. D. P. GRAHAM and the late R. ST. A. HEATHCOTE
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SOME surgeons have been of the opinion for a number of years that abdominal relaxation during operations conducted under deep ether anæsthesia is of a different quality from that found during spinal anæsthesia or the use of curare. In the latter instance the abdominal wall seems to retain some "elasticity" or resistance to displacement, whereas with ether it loses this attribute so that when retracted it stays displaced. Administration of ether during an apparently successful spinal anæsthetic produces a more complete relaxation of the abdominal muscles, characterized by loss of "elasticity". It is often quite possible to demonstrate a similar phenomenon in the theatre after curarization, though subjective assessment of the resistance of the abdominal wall of patients by the surgeon's hand has not as yet given way to more precise measurements. It is difficult to decide in such a case whether the patient is still fully curarized, or whether the curare has in part been excreted and the effect of the ether is merely an additive one on the myoneural junction.

It is generally agreed that ether, in the concentrations used for anæsthesia, has a peripheral blocking effect on neurohumoral transmission at the motor nerve ending. This effect is synergistic with that of curare. (For a review of this work and confirmation of this effect see Poulsen and Secher, 1949a.) The neuromuscular blocking action of ether is

abolished by neostigmine (Poulsen and Secher, 1949b). Part of the relaxing effect of ether on skeletal muscle may be due to its depressant effect on the excitability of peripheral nerve (Naess, 1950a), which is a definite and marked phenomenon following upon initial stimulation during the induction stages of ether anæsthesia (Naess, 1950b). Recently Secher (1951a, b, and c) has demonstrated that the peripheral effects of curare, gallamine, or decamethonium and ether on the neuromuscular junction are additive, and that ether acts preferentially on the motor end plate. Previously this author (Secher 1950) had shown that a concentration of ether (0.22 per cent) sufficient to abolish the contractions produced by indirect stimulation of an isolated muscle through its nerve did not affect contractions from direct stimulation of the muscle, which were only abolished by concentrations of 0.57 per cent of ether. He concludes that the " relaxing " effect of ether administered during anæsthesia must be exerted on the neuromuscular junction and not on the muscle substance itself.

The clinical impression suggests that ether exerts some beneficial effect in increasing abdominal relaxation even in the presence of curare. The following experiments were carried out to test whether this action might be explained by the known actions of ether in depressing spinal reflexes and exerting a peripheral neuromuscular blocking action in patients in whom the effects of curare were passing off, or whether ether exerts an effect beyond the neuromuscular junction, increasing extensibility or decreasing elastic recoil in muscle which is fully curarized.

METHOD

A series of cats was anæsthetized with chloralose 50 mg./kg. (which provides a light anæsthesia with brisk reflexes and a high blood-pressure) or pentobarbitone sodium 35 mg./kg., and

Sherrington's preparation of the gastrocnemius muscle made. The tendon was attached over a pulley to a recording lever which magnified displacement of a point on the tendon by five times and recorded it as a vertical line. The tendon was also attached by a piano wire over another pulley to a pan on to which weights were placed for 15 seconds, and from which they were quickly released and left off for 1 minute. A series of weights from 1.5 kg. was added to the pan and a record of the extension and of the elastic recoil of the muscle after quick release was made over the range in ascending and descending order. Blood-pressure was recorded from the carotid artery, anoxia avoided by using artificial respiration as needed, and d-tubocurarine 0.8 mg. injected intravenously. Ether was given either as 15 per cent vapour respired from an Oxford vaporizer or injected intravenously (as 10 per cent ether in saline) in doses of 1 ml./kg. plus 0.3 ml./kg. every ten minutes. In another series of anæsthetized cats the sciatic nerve was cut after preparation, and curare and artificial respiration given, the test carried out with the weights, and then repeated after ether and more curare. Five records of the effect of each weight were taken.

A method of direct testing of the effect of curarizing substances on the abdominal musculature was devised by Longo and Bovet (1949). Briefly, it consists of creating a pneumoperitoneum in anæsthetized animals with various measured quantities of air and recording the resistance of the system in a side tube. This method was used in a small series of cats anæsthetized with chloralose (50 mg./kg.) and the effect of gallamine 1–5 mg./kg., of ether, and of a combination of the two tested, the intraperitoneal pressure being recorded both as a direct measurement in mm. Hg from a manometer and by means of a float recorder.

RESULTS

Results of the tests on the gatrocnemius muscle are expressed in table I and illustrated in figures 1 and 2. In the first series of tests with the sciatic nerve intact and light anæsthesia the tone of the muscle varied and thus the base line of the lever varied (fig. 1A). This interfered with the taking of accurate comparative measurements of extension and elastic recoil caused by the addition and removal of weights. The scatter of the results is indicated by the large delta of the values in columns 1A and 1B of table I.

TABLE I.

Measure of extension (E) and recoil (R) of gastrocnemius muscle of choralosed cats

Weight in kg.	Nerve intact		+ curare		+ curare + ether		Nerve cut + curare		+ curare + ether	
	E	R	E	R	E	R	E	R	E	R
1	16.8 ±7.9	15.2 ±7.8	11.12 ±3.0	10.68 ±3.2	11.11 ±3.1	10.66 ±3.16	14.45 ±2.45	14.40 ±2.82	13.36 ±4.35	13.08 ±3.32
2	33.54 ±7.9	31.08 ±6.7	23.31 ±2.0	23.24 ±2.4	23.33 ±2.1	23.2 ±2.64	27.65 ±4.05	26.45 ±3.9	25.96 ±4.59	26.0 ±4.13
3	39.57 ±5.7	38.25 ±5.8	29.98 ±3.2	29.94 ±3.57	30.0 ±3.17	29.81 ±3.61	34.85 ±6.1	33.8 ±4.8	34.08 ±4.81	33.56 ±2.63
4	44.86 ±10.8	43.6 ±9.8	34.22 ±2.0	33.97 ±2.04	34.26 ±2.01	33.8 ±2.15	39.7 ±5.84	39.31 ±5.83	38.44 ±5.68	38.2 ±5.0
5	50.33 ±7.62	48.3 ±6.5	39.0 ±3.0	38.05 ±3.10	38.38 ±3.14	37.77 ±3.13	44.25 ±7.07	43.31 ±6.37	44.34 ±5.39	44.30 ±5.09
	1A	1B	2A	2B	3A	3B	4A	4B	5A	5B

Curarization (see figure 1B or columns 2A and 2B of table I) or curare and ether (see figure 1C or columns 3A and 3B of table I) abolished the tone and gave a more regular base line. The extent of extension and recoil with the weight test was significantly reduced by either procedure but no difference was observed in either extensibility or elastic recoil between the test with curare and that with curare and ether (compare 2A with 3A and 2B with 4B in table I; fig. 1B with C).

In the second series of experiments wherein the sciatic nerve was cut and curare given, records were regular (see figure 2A or columns 4A and 4B of table I) and again the addition of ether (figure 2B or columns 5A and 5B of table I) made no significant difference to the extensibility and elastic recoil of the muscle (compare 4A with 5A and 4B with 5B in table I, or figure 2A with B).

The results obtained with the Longo and Bovet technique are summarized in table II and illustrated in figure 3. They indicate that while the curariform substance gallamine ("Flaxedil") and ether lower the pressure of the pneumo-

TABLE II.

Normal		Gallamine		+ Ether	
Hg	T	Hg	T	Hg	T
5.8 ±0.38	28.0 ±1.61	4.65 ±0.16	20.74 ±1.51	4.78 ±0.1	21.8 ±1.08
1A	1B	2A	2B	3A	3B

Mean values of 20 trials with 200 ml. air in peritoneum of each of 5 cats anæsthetized with chloralose 50 mg./kg. Hg means mm.Hg pressure of pneumoperitoneum. T means extent of excursion of tambour lever. Gallamine 2 mg./kg. i.v. with artificial respiration: ether 1 ml./kg. followed by 0.33 ml./kg. every 10 minutes, given as 10 per cent solution in saline. Gallamine repeated.

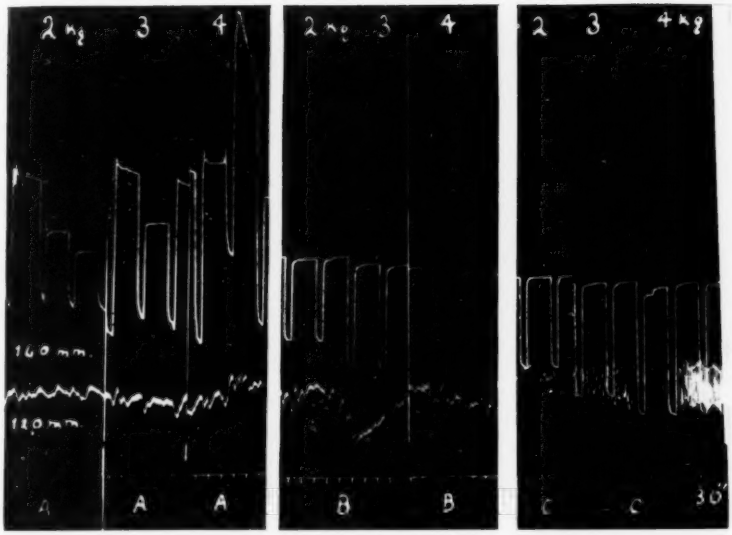

FIG. 1

Cat, male, 3.2 kg. chloralose 50 mg./kg. Upper record extension and recoil of gastrocnemius muscle caused by the addition and removal of the weights indicated in kg.: carotid blood-pressure: time in 30 seconds. In A control experiment; in B d-tubocurarine 0.8 mg. injected intravenously; in C ether 15 per cent in air inhaled for 20 minutes and curare repeated.

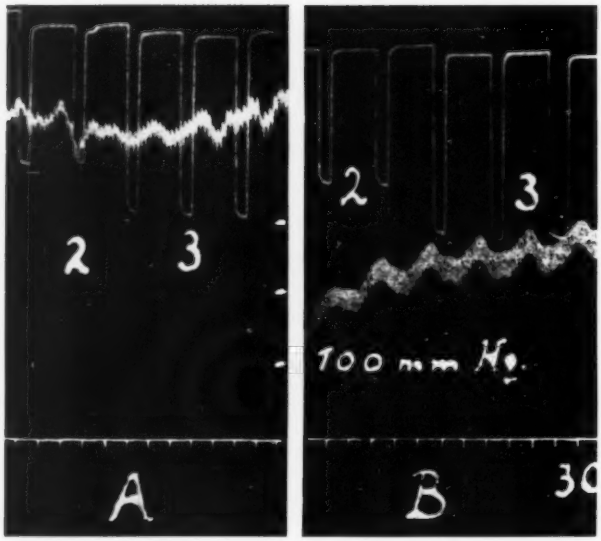

FIG. 2

Cat, male, 2.8 kg., chloralose 50 mg./kg. Preparation as in figure 1, but with sciatic nerve cut. In A d-tubocurarine 0.8 mg.; in B ether 1 ml./kg. as 10 per cent solution in saline injected i.v. 15 minutes previously, plus 0.33 ml./kg. every 10 minutes and curare repeated.

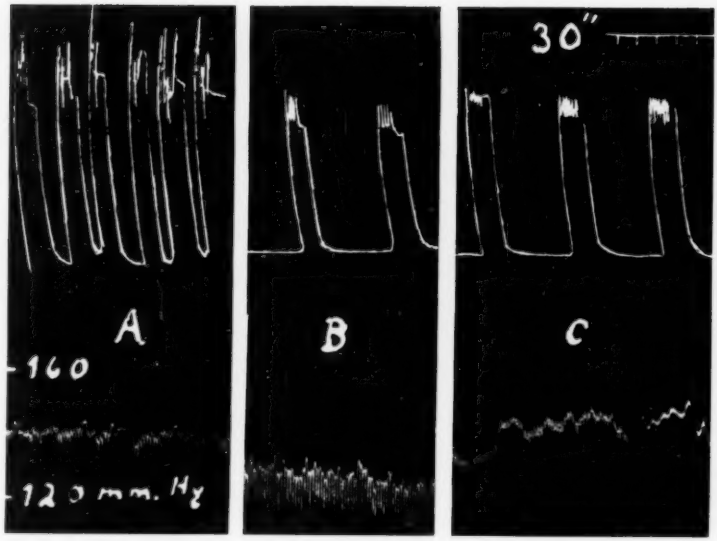

FIG. 3

Cat, male, 2.9 kg., chloralose 50 mg./kg. Upper record excursion of tambour connecting with pneumoperitoneum of 200 ml., lower record carotid blood-pressure. Time in 30 seconds. In A chloralose only; in B gallamine 2 mg./kg. i.v. with artificial respiration; in C after gallamine and ether 1 ml./kg. i.v. as 10 per cent solution in saline, plus 0.33 ml. every 10 minutes. Record begun at 21 minutes after ether commenced, 5 minutes after gallamine.

peritoneum (compare table II columns 1A with 2A and 3A) and reduce the excursion of the tambour attached to it (compare table II 1B with 2B and 3B, or figure 3A with B and C) there is no further relaxing effect of ether in a fully curarized abdomen (compare table II 2A with 3A or 2B with 3B and figure 3B with C).

DISCUSSION

These experiments support the work of Secher (1950) who had concluded from studies on the isolated nerve-diaphragm preparation that ether in concentrations great enough to block neuromuscular conduction did not affect the muscle itself. We have found no evidence that large amounts of ether (up to 15 per cent in inhaled air for 20 minutes or 1 ml./kg. body weight injected, with "boosting doses" of one-third that amount) exert any effect upon the extensibility and elasticity of muscle which has been severed from the central nervous system by curarization. If, however, the curarization is inadequate or sufficient time has elapsed for its effects to begin to pass off, there is every evidence that addition at such a time of ether will further relax the partially paralysed muscle. This additive effect of curare and ether is well known and doubtless explains the clinical phenomenon mentioned at the beginning of this paper.

In the lightly anæsthetized cat with motor nerve intact the extension of the muscle produces myotactic reflexes which are abolished by etherization or curarization. Ether in anæsthetizing concentrations thus exerts a pharmacodynamic action on the central nervous system, on the nerve, and on the neuromuscular junction, but not apparently on the muscle substance.

SUMMARY

In chloralosed cats ether does not affect the extensibility or elastic recoil of gastrocnemius muscle which is paralysed by curare. The pressure of a pneumoperitoneum (indicative of the state of the abdominal musculature) likewise is not affected by ether if curarization is complete. If curarization is passing off ether has an additive effect and relaxes the muscle to its former state of paralysis. This probably accounts for the clinical phenomena discussed.

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TENSILON: A NEW ANTI-CURARE AGENT

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WHILE it is true that antidotes to the curarizing drugs are regarded with suspicion in some quarters, there is no doubt that most anæsthetists would not like to be without an agent of this type permanently. The currently available drug is " Prostigmin " (neostigmine B.P.) which when given in adequate dose and with sufficient atropine will produce permanent reversal of the muscle-paralysing action of the d-tubocurarine and other like substances. There have, however, been reports of cases in which it seemed possible, though it was by no means certain, that the muscarinic action of the neostigmine might have been responsible for fatalities (Macintosh, 1949 ; Clutton-Brock, 1949).

When, therefore, the drug Tensilon became available and appeared to be comparatively free from such dangers it seemed as if there was no longer any need to subject patients to the possible risk that the quantity of atropine given with the neostigmine might not be sufficient to control unwanted side-effects.

Tensilon (3 hydroxy-phenyl dimethyl ethyl ammonium bromide) was selected by Randall (1950) from a group of related compounds as that possessing the greatest anti-curare activity and the least marked muscarinic effect. Its action was examined in detail by Riker et al. (1949), Wescoe et al. (1949, 1950), Artusio et al. (1950), Riker and Wescoe (1950), and others. It was shown to be effective in reversing the muscle-paralysing action of d-tubocurarine, both in experimental animals and in man. It also, in twenty

times the de-curarizing dose, could itself produce a myoneural block similar to that induced by decamethonium. It possessed little anticholinesterase activity but did have a mild depressor action on the dog, probably as a result of its chemical similarity to acetylcholine. Its depressor action was converted to a mild pressor action by atropine. In man its action on the blood-pressure and pulse rate was comparatively slight. It thus seemed as if it would prove the ideal decurarizing agent. An extended investigation of its effects in patients curarized with di-methyl tubocurarine and gallamine triethiodide was therefore desirable. No attempt was made to use it as an antidote to decamethonium as Randall (1951) had already found it to be useless in this respect.

The first step in the investigation was obviously to make certain in the laboratory that Tensilon was as effective as an antidote to gallamine triethiodide as it was to d-tubocurarine. Since the reason for giving decurarizing drugs in the human subject is to restore respiration, the effect of Tensilon on the breathing of curarized cats and dogs under pentobarbitone anæsthesia was studied. It was found that the drug would reverse both complete apnœa and respiratory depression due to gallamine triethiodide. Further, the diaphragmatic and intercostal components of respiration recovered together as they do when neostigmine is given. The effect of Tensilon on the blood-pressure of the cat was similar to that noticed by Riker and his colleagues (1949) in their experiments. When the drug was given alone there was sometimes a small evanescent fall in blood-pressure. When it was given with atropine there was a temporary slight rise in blood-pressure. This brief investigation seemed to indicate that Tensilon would be as effective against curarization due to gallamine triethiodide as it was against

that due to d-tubocurarine. In view of the close chemical similarity between this latter drug and its di-methiodide it scarcely seemed necessary to confirm the effectiveness of Tensilon as an antidote to the latter drug in the laboratory. Tensilon was, however, tested as a decurarizing agent against Win 2747 (Hoppe, 1950) in the laboratory and it was found to be ineffective.

DECURARIZING ACTION OF TENSILON IN MAN

Methods. The decurarizing action of Tensilon was studied in 55 patients; 17 of these were curarized with d-tubocurarine, 8 with di-methyl tubocurarine, and 30 with gallamine triethiodide (Flaxedil). The numbers of cases in these groups do not give an adequate indication of the depth of curarization involved, but in table I will be found the doses of these drugs used by the author in a previous series of abdominal operations where an attempt was being made to estimate the equivalent doses of curarizing agents; wherever it was necessary an additional dose of relaxant was given to facilitate closure of the abdomen.

TABLE I
The Dosage of Relaxants for Abdominal Operations.

Drug		Dosage		
		Operation up to 30 mins. (mg.)	Operation 31 – 60 mins. (mg.)	Operation 61 + mins. (mg.)
d-tubocurarine	Mean dose	16	26	34
	Range	(10 — 30)	(15 — 45)	(20 — 50)
dimethyl tubocurarine	Mean dose	9	11	19
	Range	(6 — 11)	(4 — 18)	(8 — 33)
gallamine triethiodide	Mean dose	84	111	160
	Range	(60 — 100)	(80 —160)	(90 —240)

The figures in parenthesis indicate the range of dosage in each group. The mean number of cases on which each of these observations are based is 14.2 and the range 4—26.

All cases were anæsthetized with nitrous oxide and oxygen after a barbiturate induction. Supplementary analgesic drugs were given where necessary, with the result that most of the patients recovered consciousness very promptly when the anæsthetic was stopped. It was thus very often possible to test the degree of recovery from the curarizing drug by the ability of the patient to open his eyes in response to a command, or by his pulling a face when his supraorbital nerve was compressed. Return of the lid reflex was also sought, though it was not invariably present, even in patients who could speak. The quality of the spoken word was observed and the disappearance of the thick speech of partial curarization regarded as further evidence of complete recovery. Even before the patient had recovered so completely it was often possible to tell whether decurarization was complete. Thus the abolition of chin tugging and the return of full intercostal respiratory movement gave a fairly reliable guide. The restoration of completely effective coughing in response to movement of the endotracheal tube was also fairly conclusive evidence of complete decurarization, as was the appearance of rigidity of the abdominal wall as the patient strained on his tube. On the basis of these criteria it was possible to sort out the results obtained into cases of complete decurarization, cases of partial decurarization, and failures.

At first it was accepted, mainly on the basis of the experience of the case described in the section on side-effects, that the maximum safe dose of the drug was 10 mg. Later, however, it was found possible, with suitable modification of the dose of atropine, to increase the dose of Tensilon to 20 mg. with complete safety. This dose, however, was usually given in two fractions of 10 mg., or even three fractions of 10, 5 and 5 mg., rather than all at once. A child of 9 years of age

whose weight was 4 stones received her Tensilon in doses of 5, 2.5, and 2.5 mg. Atropine was dissolved in the Tensilon and given simultaneously with each dose so that not more than 1/100 gr. (0.65 mg.) of this drug was administered to any single patient.

Results. The results obtained are set out in the appended tables II, III and IV. It will at once be apparent that even in doses of 20 mg. Tensilon is not a decurarizing agent of reliability comparable to that of neostigmine bromide.

TABLE II
The Effectiveness of Different Doses of Tensilon.

Dose of Tensilon (mg.)	Degree of Decurarization after Tensilon		
	Complete	Partial	Negligible
5	1	—	—
10	27	5	1
15	5	1	—
20	12	3	—

There were too many cases in which its effect was incomplete. This incompleteness had several interesting associations. Thus the drug was most effective where the curarization was mild and had already decreased to the stage of slight respiratory depression. It was very unreliable in patients whose spontaneous respiratory activity had been nearly abolished (table III) by the curarizing agent. Tensilon too seemed to be a more satisfactory decurarizing drug

TABLE III
The Effectiveness of Tensilon as an Antidote at Various Depths of Curarization.

Degree of Curarization before Tensilon	Degree of Decurarization after Tensilon		
	Complete	Partial	Negligible
Deep	5	3	1
Moderate	19	3	—
Mild	16	—	—

in cases to whom the relatively short acting drugs, gallamine triethiodide and dimethyl tubocurarine, had been given and to be less valuable in producing permanent reversal of the rather longer acting d-tubocurarine (table IV). There was another interesting feature of the action of Tensilon in that

TABLE IV

The Effectiveness of Tensilon as an Antidote to Various Curarizing Agents.

Curarizing Agent	Degree of Decurarization		
	Complete	Partial	Negligible
d-Tubocurarine	11	5	1
Dimethyl Tubocurarine	7	1	—
Gallamine Triethiodide	26	4	—

very often more or less complete decurarization followed the administration of the first dose of the drug and then a relapse into partial curarization occurred. This relapse could be reversed by a second dose, but in some cases a third dose was required before permanent and complete decurarization was produced. The interval between these successive doses was often such that there was some doubt as to whether the degree of recovery finally obtained was not due in part at least to spontaneous elimination of the curarizing drug.

Side-effects. Since Tensilon had a close chemical similarity to acetylcholine and neostigmine it seemed advisable to give atropine with it. When this was done the blood-pressure changes which occurred were small (table V). Further, they nearly always righted themselves spontaneously in a few minutes. Indeed the only case in which anxiety was caused by the hypotensive action of Tensilon was a woman in whom 10 mg. given with 1/100 grain (0.65 mg.) of atropine had failed to produce adequate decurarization.

TABLE V

The Blood-pressure Changes caused by Tensilon given with Atropine.

	Blood-pressure Changes		
	Rise	Nil	Fall
Number of Cases	3	8	26
Mean change (mm. Hg.)	16	—	15.8 ± 8.1 (Range 5-30)

A second 10 mg. was given, in this case without additional atropine, and the blood-pressure fell from 105 mm. to 70 mm. Hg in two minutes. A second 1/100 grain (0.65 mg.) of atropine with 10 mg. of Methedrine were then given and the blood-pressure level was restored to 90 mm. Hg, though only at the expense of producing a severe tachycardia. Subsequent experience indicated that the administration of a total dose of atropine of 1/100 grain (0.65 mg.) was sufficient to prevent major blood-pressure changes and since this policy has been adopted side-effects have been minimal.

The changes in the pulse rate have been of equally little significance. The general tendency was for the pulse rate to settle at a level of about 100 per minute. Thus in cases where the pulse had already been accelerated by gallamine triethiodide there was a tendency to slowing, and where the pulse rate was already slow in cases to whom d-tubocurarine or its di-methiodide had been given there was an acceleration. The actual figures for the cases for which the information is available are: pulse rate unchanged 6 cases; pulse rate slowed 16 cases; pulse rate accelerated 15 cases.

The changes in pulse rate after the administration of Tensilon with atropine differ markedly from those produced by neostigmine and atropine (figs. 1 and 2). When this latter combination of drugs is given there is always an

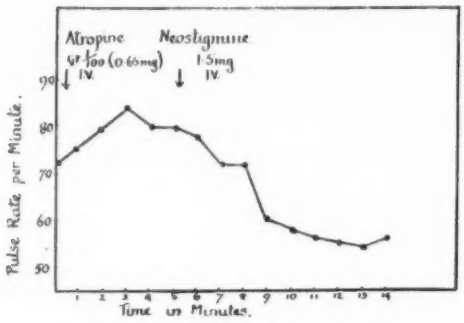

FIG. 1

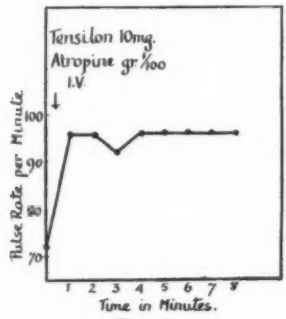

FIG. 2

initial cardioacceleration, most marked when 1/50 grain (1.3 mg.) is the dose of atropine. This is followed by a slowing of the pulse rate. The bradycardia is never extreme when this dose of atropine is used, but may be alarming if only 1/100 grain (0.65 mg.) of atropine is given. When Tensilon is given with 1/100 grain (0.65 mg.) of atropine the bradycardia does not occur. The pulse rate settles almost immediately at about 100 per minute and no further change appears.

Spirometric Studies. The use of the respiratory depression as a measure of curarization is open to criticism, on the ground that it is possible for diaphragmatic over-action

to compensate for the loss of ventilation produced by intercostal paralysis. None the less Artusio and his colleagues (1950) used this criterion in his study of the action of Tensilon and some related substances. It therefore seemed as if it might be worth while to repeat some of his investiga-

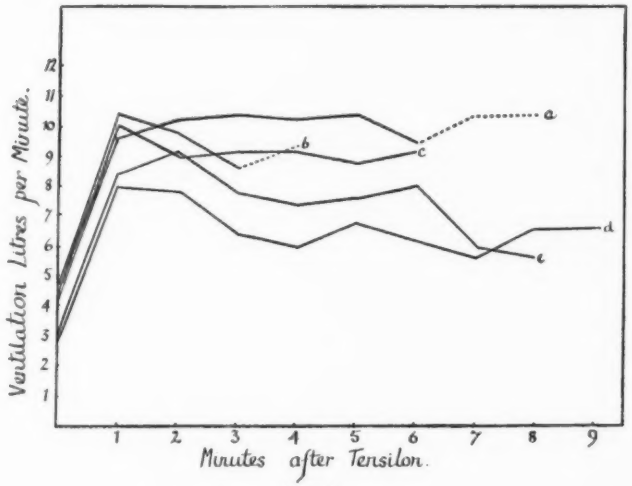

FIG. 3

Changes in ventilation per minute after the administration of Tensilon.

Curve *a*: 10 mg. initially and 10 mg. at 6 minutes.
Curve *b*: 10 mg. initially and 10 mg. at 3 minutes.
Curve *c*: single dose of 20 mg.
Curve *d*: single dose of 10 mg.
Curve *e*: single dose of 10 mg.

tions. For this purpose patients were connected to a closed-circuit apparatus through which only a basal flow of oxygen was running. On the expiratory side of the circuit there was inserted a wet gas meter, and with the aid of this the patients' ventilation per minute was measured. These studies added nothing to the evidence of decurarization

obtained from clinical observations reported above, particularly as they could be applied only to patients whose breathing was already forcible enough to ensure that serious anoxia would not occur during the period of measurement. The results are shown graphically in figure 3 and do give numerical confirmation of the fact that the decurarization produced by Tensilon is maximal immediately after its administration; thereafter in some cases curarization tends to return, but the same degree of recovery can be produced by a second dose of Tensilon.

DISCUSSION

The most immediate conclusion to be drawn from this study is that Tensilon is not a completely satisfactory decurarizing agent in man in that the effect of a single dose tends to wane shortly after its administration. Adequate decurarization can probably be produced by a series of doses of the drug, but as there is already a completely satisfactory single-dose antidote to curarization in neostigmine bromide there would seem to be little justification for the use of Tensilon on this ground. The case for the employment of Tensilon rests on the relative absence of side-effects after its administration. If it is considered that the secondary bradycardia which appears in cases to whom neostigmine bromide has been given is an indication that complete cardiac inhibition will one day occur in a patient with pronounced vagal tone, then Tensilon is the preferable decurarizing agent. If, however, it is believed that 1/50 grain (1.3 mg.) of atropine affords adequate protection against the muscarinic activity of neostigmine, then this more certain antidote will obviously be the anæsthetist's choice for the curarized patient.

No very direct evidence concerning the mode of action of

Tensilon has emerged from this study, but its findings are readily explained in terms of what is already known about its action. It has been demonstrated electronically that Tensilon converts each successive muscle response to a nerve impulse, from a single twitch to a short tetanus. This action is not peculiar to Tensilon but is shared by eserine and neostigmine. There is, however, an important difference between Tensilon and the other drugs. The anticholinesterases produce their repetitive action by interfering with hydrolysis of acetylcholine produced at the nerve ending, with the result that there is still an effective concentration of this substance at the myoneural junction at the end of the refractory period of the muscle fibre. Tensilon on the other hand has a relatively insignificant anticholinesterase activity (Cohen and Unna, 1951) and produces its anti-curare effect by causing an increase in the sensitivity of the muscle fibre to normal amounts of acetyl choline. It is of interest that this stimulant effect on muscle contraction is not confined to curarized muscle. When injected into normal patients Tensilon temporarily increases the force of muscle contraction and may cause muscular fasciculation and result in deviation of the eyes into abnormal positions (Westerberg et al., 1952). On the other hand because the drug possesses only slight anticholinesterase activity its action on the circulatory system tends to be immediate and short acting. Further, there is none of the secondary muscarinic activity which characterizes the action of neostigmine.

The final conclusion would seem to be that neither neostigmine nor Tensilon is the perfect decurarizing agent. The former gives rise to unwanted muscarinic effects which require for their control the administration of large doses of atropine, and the latter drug is too evanescent in its action

to be of much use in single doses, though it seems to be possible that multiple injections may prove to be relatively satisfactory. Tensilon may, however, point the way to the synthesis of the perfect anti-curare agent by indicating that this might well be a drug of similar structure which is less readily inactivated in the body.

SUMMARY

The anti-curare action of Tensilon (3 hydroxy-phenyl dimethyl ethyl ammonium bromide) has been investigated. It was found that the effect of this drug, though apparently complete and permanent in experimental animals, was somewhat evanescent in man. If complete decurarization was to be maintained in the human subject it was often necessary to give second or even third doses of Tensilon. Circulatory side-effects were slight when atropine was given with Tensilon. The conclusion is drawn that Tensilon, though free from the more serious muscarinic actions of neostigmine, is not as reliable an antidote to the muscle paralysing action of d-tubocurarine.

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EARLY USE OF ROTAMETER IN ANÆSTHESIA

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THE rotameter has gained widespread use for measuring the flow of gases and liquids in industry. It is also extensively used in anæsthetic practice.

Mr. Karl Küppers of Aachen applied for a German patent on this flowmeter in 1908, which was granted on December 15, 1909 (Küppers, 1909). He had worked out the scientific principles of the apparatus at the Chemical Technical Institute of the Aachen Hochschule (Anonymous, 1910a; Neu, 1910a). Mr. Küppers had obtained patents first for a burner which produced a flame of high temperature. To produce this blue flame for incandescent light or heating purposes it was necessary to bring together two gases in a given volume relationship. It seems quite probable that Mr. Küppers later invented the rotameter as a measuring device to indicate the relationship of the two gases flowing into the burner.

The commercial production of the flowmeter was undertaken in 1909 by the Rotawerke at Aachen under the name Rotamesser. The name of the company was changed to Deutsche Rotawerke on July 1, 1910, when Mr. Felix Meyer took over its management (Handelsregister, 1910). Shortly following the beginning of commercial manufacture two rotameters were sent to the School and Experimental Gas Institute of the German Society for Gas and Water Specialists in Karlsruhe, which was under the

direction of Professor Karl Bunte. Here the flowmeter was studied and tested and a report was made describing the scientific basis for the accurate measurement of gas flows by the instrument and enumerating its possible applications (Bunte, 1910). This report apparently formed the basis of subsequent announcements and articles on the rotameter (Anonymous, 1910b, c, d, 1911a, b, c, d, 1913; Meyers, 1910; Strache, 1913; Bertelsmann, 1911). The flowmeter was also studied at the Chemical Laboratory of the Clay Industry in Berlin and a report was made to the Society of German Manufacturers of Fire-Proof Products on February 16, 1910 (Cramer, 1910).

Dr. Maximilian Neu

Dr Maxmilian Neu of the Heidelberg Women's Clinic adapted the rotameter to provide a known volume percentage relationship of nitrous oxide–oxygen during anæsthesia. Neu attended the February 22, 1910, meeting of the Natural History Medical Society of Heidelberg held in the auditorium of the Pharmacological Institute (Offizielles Protokoll, 1910). At this meeting Professor R. Gottlieb spoke on the advantages of nitrous oxide–oxygen anæsthesia combined with morphine scopolamine premedication; and his associate, W. Madelung, demonstrated the action of nitrous oxide–oxygen anæsthesia on rabbits premedicated with morphine and scopolamine. Evidently Neu was already interested in this type of anæsthesia as he is listed as one of those who took part in the discussion along with Gottlieb and Medelung. At the following meeting of this society held on July 26, 1910, Dr. Neu presented a paper entitled "A Method of Nitrous Oxide–Oxygen Anæsthesia" and demonstrated the use of the rotameter for a patient during an operation (Neu, 1910a, 1910b). Neu first

acknowledges the work of Gottlieb and Madelung with combined nitrous oxide–morphine–scopolamine anæsthesia. He states that "some time ago Mr. Küppers of Aachen was able to construct an apparatus to measure gas which bears the name 'Rotamesser' and which serves to indicate the consumption of gas in a simple way. The scientific principle of the apparatus was worked out at the Chemical Technical Institute of the Aachen Hochschule (Professor Rau)". He then describes the principle of the apparatus. Further he states that "Herr Professor Bunte in Karlsruhe has just recently tested the apparatus in his experimental gas institute and found that the readings of the rotameter are correct. . . . By means of this apparatus, it was now an easy thing to produce an accurate mixture of nitrous oxide and oxygen. In particular, an apparatus must have the ability to produce a mixture according to percentage of volumes, and the Rota-apparatus provides exactly a mixture of gases in fixed volume ratio. A postulate of pharmacology is also realized according to which only an apparatus which conveys the complete dosage mixture directly to the airway gives actual and certain control over the concentration of anæsthetics in the atmosphere of the lungs". An illustration shows the arrangement of the apparatus.

He continues: "If I, for example, place the apparatus so that the float of the oxygen meter is on 1, and that of the nitrous oxide meter stands on 4, then I have a percentage volume relationship of 20:80, that is, I allow the apparatus to measure for a unit of time of one minute; therefore 1 litre of oxygen and 4 litres of nitrous oxide flow through the measuring tube in the minute. By means of the apparatus I am in a position to multiply the consumption relationship, whereas the percentage relationship remains the same. I

can thus, for example, allow 2 litres of oxygen and 8 litres of nitrous oxide per minute to flow through. With that the volume relationship naturally remains unchanged. With the arrangement which I demonstrate to you we were in a position to allow exact dosage mixtures of gas to flow to the patient. We have gradually learned to accomplish N_2O–O_2 anæsthesia with complete depth." Further on he states that he is already occupied in designing a scientific apparatus to analyze the blood circulation during anæsthesia. A footnote states that the Rotawerke at Aachen has undertaken the construction of such an apparatus. The apparatus is not described and a careful search of his subsequent writings does not reveal a record of any further work on this subject. The use of the rotameter to measure blood-flow rates was reported by Gregg et al. in 1942.

Neu gave his second demonstration of the new apparatus and a paper at the 82nd Meeting of the German Society of Scientists and Physicians held at Konigsberg on September 20, 1910 (Neu, 1911a, 1911b). He first refers to the advantages of combined morphine–scopolamine–nitrous oxide–oxygen anæsthesia based upon the research of Gottlieb and Madelung. He then goes on to state: " The hypothesis for a rational application to man was to find a method able to produce an exact dosage and a variable gas mixture. This postulate the author was able to fulfill. The author availed himself of Mr. Küppers of Aachen for the construction of the anæsthetic apparatus along with the gas measuring apparatus which bears the name Rotameter and therefore serves, in a simple manner, to indicate the gas flow. With the help of this apparatus an exact dosage mixture of nitrous oxide–oxygen in the desired percentage of volume could be produced. Apparatus for pure nitrous oxide, nitrous oxide–air, and nitrous oxide–oxygen anæsthesia

has existed in quantity in America, the land of laughing gas anæsthesia, for quite some time, but none of this apparatus renders possible the measurement of the gas and the variation of the mixture of the gas. The essential importance and newness of the apparatus lies in the carry-over of measurement of gas into the technique of nitrous oxide anæsthesia and in the development of the principle to vary momentarily the percentage mixture of gas. By means of the combined method of morphine–scopolamine, nitrous oxide–oxygen anæsthesia and of the new apparatus 41 anæsthetics were given."

The paper was discussed by Gottlieb of the Pharmacological Institute of Heidelberg who reported his work with Madelung on the increased effectiveness of nitrous oxide–oxygen anæsthesia on animals following premedication with morphine and scopolamine. He recommended the apparatus of Neu since it would provide exact dosages in the application of this research to man.

Neu again demonstrated his apparatus at the Natural History Medical Society of Heidelberg on February 7, 1911 (Neu, 1911c). " Mr. Neu demonstrated his useful apparatus for nitrous oxide anæsthesia. He gave first of all a technical communication on the apparatus. The apparatus stands on a nickel-plated and movable table to which the nitrous oxide and oxygen tanks can be attached. On the tank is a reducing valve through which at the same time the gas capacity in the tank is controlled. The gas passes through the rotameter to a mixing bag, which can be closed by a stopcock. The apparatus is so built that it can be readily combined with the Tiegel-Henschen positive pressure attachment for intrathoracic surgery. . . . The Deutsche Rotawerke in Aachen which undertakes the manufacture and distribution of this useful anæsthesia apparatus,

guarantees the exact calibration of the rotameter tube." He then mentions the high price of nitrous oxide which up to then had only been made in England and America, and expects that the German chemical industry will soon undertake the manufacture of nitrous oxide and thus reduce the price.

Dr. Neu demonstrated his apparatus and delivered an extensive paper on nitrous oxide–oxygen anæsthesia at the 40th Congress of the German Society of Surgery on April 22, 1911, at Berlin (Neu, 1911d, 1911e) in which he repeated previous observations and stressed the following advantages of the machine: "The action of the rotameter is stabilized by the rotation of the specially built float. Suitably engraved white spiral lines on the float make its movement perceptible to the eye. The graduation in litres flow rate per minute is fixed empirically during calibration of the tubes. The adjustment is reached quickly and easily. Thus a momentary and certain variation of the dosage is guaranteed. The Deutsche Rotawerke in Aachen build the apparatus and guarantee the exact performance of the metering tube."

Maximilian Neu was born in 1877. At the time of his writing he was a lecturer at the University of Heidelberg and an assistant at the Women's Clinic. At some of the medical meetings where he demonstrated his apparatus, he also delivered papers on obstetrics and gynæcology. He wrote many papers in these two fields, the last of which is listed for the year 1929. He was a member of the German Society for Surgery and is listed as a member up to 1935. He died on October 22, 1940, in Heidelberg. It has not been possible to find an obituary notice in the medical literature.

Lack of Widespread Use

Following Neu's demonstrations, others employed the Rotameter anæsthesia apparatus manufactured by the Deutsche Rotawerke and reported on its use (Schlimpert, 1912; Zweifel, 1913). Some writers said that nitrous oxide–oxygen anæsthesia could not produce adequate relaxation for abdominal operations. Neu insisted this was not the fault of the apparatus but that the nitrous oxide–oxygen anæsthesia combined with morphine and scopolamine could produce sufficient abdominal wall relaxation if skilfully administered (Neu, 1912). However, since the Rota apparatus did not provide for the giving of ether, this was considered a disadvantage. The apparatus was expensive, being almost twice the price of other types. Nitrous oxide gas at that time was only beginning to be made in Germany; and most of it being imported was expensive. Apparatus for giving ether was cheaper and therefore preferred. Since nitrous oxide was not used extensively in Germany, widespread interest in Neu's rotameter apparatus for the accurate measurement of gas flows did not develop.

Subsequent Adaptations of Rotameter to Anæsthesia

Following encouraging research on animals, Gauss and Wieland introduced acetylene into clinical practice in 1922 (Gauss and Wieland, 1923a). For the first 163 acetylene anæsthetics a Neu-Rota nitrous oxide apparatus was recalibrated by Wieland for use with acetylene. The first apparatus specially built for acetylene anæsthesia was made by Dragerwerk, Lubeck. This apparatus incorporated a rotameter for the measurement of the flow rate of the acetylene-oxygen mixture. Several illustrations of the apparatus exist in the reports of acetylene anæsthesia

(Mallebrein and Maier, 1925; Schligen, 1924; Gauss and Wieland, 1923b).

Until 1939 the rotameters used on anæsthetic apparatus in England were obtained by Trost Brothers Ltd. from the Deutsche Rotawerke in Aachen for whom they acted as sales agents. This Deutsche Rotawerke was the same company which had built the rotameter anæsthesia apparatus for Dr. Maximilian Neu in 1910.

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ROTAMETERS IN ANÆSTHESIA

By Ernst Trier Mörch

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ROTAMETERS for many years have been used in technical work, e.g. in gasworks to measure large amounts of streaming gases. The diameter of the meter varies in size, depending on the purpose, and is often from inches to some feet. In the case of very large flows the gas is measured by means of a rotameter in a small shunt and the total flow then calculated. The rotameter was designed by Küppers in Aachen, Germany, probably shortly before 1910.

At that time Dr. M. Neu of Heidelberg, Germany (1910), was looking for a way to obtain exact mixtures of gases for clinical anæsthesia. He found that with the rotameter " it was an easy matter to produce an exact anæsthetic mixture of nitrous oxide and oxygen " (" *war es nunmehr ein Leichtes, ein exakt dosiertes Narkosengemisch von Stickoxydul und Sauerstoff herzustellen* "). He constructed an apparatus for clinical anæsthesia and stated in his first publication of it that his apparatus was self-explanatory from his illustration, a rather poor photograph. A brief description and a good picture (fig. 1) of Neu's apparatus, manufactured by " Die Deutschen Rotawerke in Aachen ", is given in von Brunn's textbook on general anæsthesia (1913).

Each gas flows from a steel cylinder with reducing valve (V), through tubing to a rotameter (R), about 2–3 feet high,

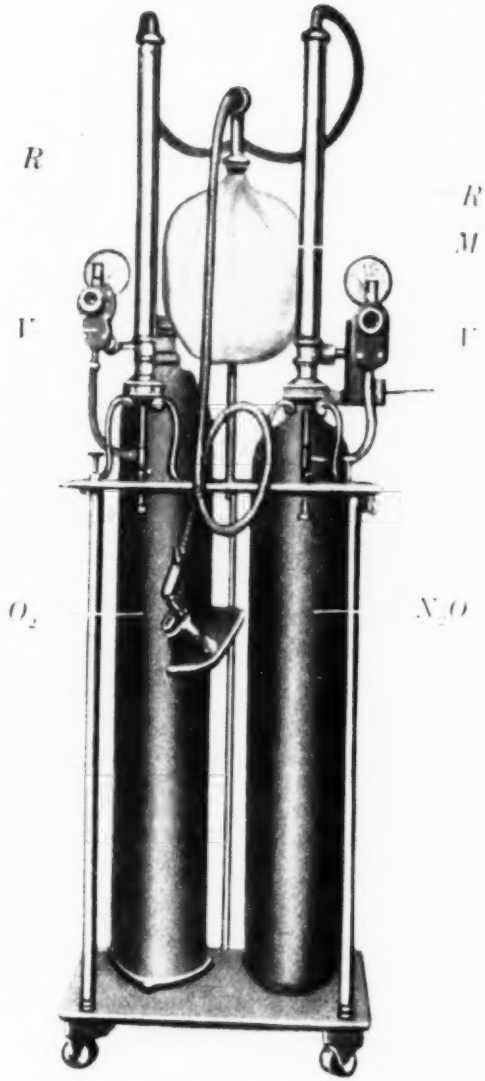

FIG. 1

Neu's anæsthetic apparatus (1910) with Rotameters (after v. Brunn).

and from here to a breathing bag (Respirationsbeutel), M, where the gases are mixed. A single large-bore tube connects the bag to a face mask equipped with an escape valve.

The physical working principle of the rotameter is given based upon Küppers' description (1910): The gas streams up through a vertical tube in which the bore gradually increases, lifting a "rotor", a rotating bobbin (*ein Schwimmer*) to varying levels depending on the velocity of the gas. Part of the gas streams through small oblique grooves in the cylindrical part of the circumference of the rotor, causes it to spin, keeps it vertical and prevents it from adhering to the wall. The spinning of the rotor is more easily determined because of a white spiral line painted on the side of the rotor. The calibration is done empirically and individually for each glass tube.

Neu (1910) used the apparatus for different gynæcological operations, even for such major procedures as abdominal hysterectomies, and with good results.

The premedication was rather heavy; on the evening before the operation the patient received Veronal (Barbital, diethylbarbituric acid) 0.5–1 g. Two hours pre-operatively hyoscine 0.4 mg. (1/150 grain), and morphine 8 mg. (1/8 grain) were given subcutaneously, and half an hour before the operation another injection of hyoscine 0.3 mg. (1/120 grain) and morphine 10 mg. (1/6 grain) was administered (von Brunn, 1913).

Neu used flows of 1 litre of oxygen and 4 litres of nitrous oxide and allowed some rebreathing, or flows of 2 and 8 litres with no rebreathing. With both techniques he maintained about the same oxygen percentage.

Neu explained the working of the rotameter as follows: the rotor is lifted until the force exerted by the streaming gas (i.e. the drop in pressure around the rotor) is the same

as the weight of the rotor; or expressed in another way the rotor ascends to a level where the space around it is so large that the drop in pressure equals the weight of the rotor.

A more dense gas requires a larger space for a certain flow to exert the same drop in pressure; if run through the same meter it would thus lift the rotor higher and apparently show a greater flow.

For his calculations Neu applied the following formula from Küppers:

$$A = \tfrac{1}{2} M.v^2$$

where A is the force the gas must exert to lift the rotor, M is the mass of the gas, and v is the velocity which, in this case, is proportional to the volume, V. Provided that the same meter is used, the force required to keep the rotor at a given level is the same regardless of the gas used. For two different gases he then applied the formula:

$$M\,V^2 = M_1\,V_1^2 \quad \text{, or}$$

$$\frac{V}{V_1} = \sqrt{\frac{M_1}{M}}$$

This formula by Küppers (1910) presents a much too simple picture of the relationship between velocities and densities of the gases. Küppers' formula assumes that a certain mass of the gas loses all its energy, but actually it loses only part. When the rotor is in equilibrium the condition represents largely a change of energies, from potential to kinetic.

Küppers' formula might suggest the erroneous inference that a rotameter calibrated for one gas could be

used for another gas by use of his formula. Clark (1952) has pointed out that this is not the case, and that the rotameter must be calibrated separately, empirically for each gas.

Küppers' formula is too simple, even if one ignores such more or less minor quantities as the compression of the gas, thermal effect, viscosity, and the difference in velocity patterns (streaming curves) of different gases, which may be appreciable.

Küppers' formula requires that under all conditions the velocity must vary inversely as the square root of the density. This is not so, because if the rotor is chosen so that the density of the rotor is twice that of the gas, then a variation in density of the gas does not involve any change in velocity (Eckman, 1950).

To demonstrate that density may have an effect, Clark (1952) has used a more complicated formula, derived from Bernoulli's equation, which still ignores all the above-mentioned, and other variables:

$$\frac{(v_2^2 - v_1^2)_a}{(v_2^2 - v_1^2)_b} = \frac{d_b}{d_a}$$

where a and b refer to the respective gases, d = density, v = velocity. 1 refers to the bottom of the rotor, and 2 refers to the top of the rotor.

Variations in the temperature or the atmospheric pressure do not influence the readings very much. If the atmospheric pressure increases, the readings will increase slightly, because the gas is compressed slightly and the weight per volume is increased by the pressure. During ordinary variations in the atmospheric pressure, however, this fault is insignificant.

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VINYL ETHER*

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HISTORY

Semmler in 1887 first described a substance which he believed to be di-vinyl ether. He prepared it from vinyl sulphide and silver oxide, and found its boiling point to be 39°C.

In 1931 Ruigh and Major were unable to repeat this process, but they synthesized vinyl ether by another method, and found it had a boiling point of 28.3°C. This latter substance differs somewhat from Semmler's original preparation, which was probably impure.

In 1930 Leake and Chen made a study of anæsthetic properties, and their relationship to chemical structure in the hydrocarbons. They forecast the discovery of a substance with the approximate formula of vinyl ether, and hoped it would combine the potency of di-ethyl ether, with the rapidity of induction, and the low toxicity of ethylene.

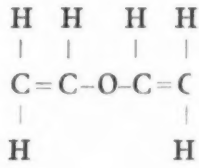
As soon as pure vinyl ether had been prepared in 1931, investigations were made into its pharmacological properties by Leake and his associates (1933), and in 1933 Gelfan and Bell reported the first three experimental administrations in man, and recommended further clinical trials. Since then there has been a wealth of both experimental and clinical

* An essay in partial fulfilment of the requirements of the Diploma Course in Anæsthesia, Department of Anæsthesia, McGill University, Montreal, Canada.

investigation, reaching its peak in the late 'thirties. Vinyl ether was found to have the properties predicted, but eventually certain drawbacks were discovered, and now it has found its own place among the anæsthetic agents, with well-established uses and contra-indications, and the intense interest which its discovery first evoked has subsided.

CHEMICAL PROPERTIES AND FORMULA

Vinyl ether is a symmetrically unsaturated aliphatic ether (Adriani, 1946) derived from vinyl alcohol. Its formula is:



It is very volatile and easily oxidized. On exposure to light and air, it decomposes to aldehydes, organic oxides, and acids, with subsequent polymerization of these substances to form resins. It does not affect (Adriani and Rovenstine, 1941) and is unaffected by soda lime, and is therefore quite suitable for use in a closed system with absorption techniques.

Commercial Vinesthene consists of di-vinyl ether with 3.5 per cent of absolute alcohol added to render it less volatile and to prevent freezing on evaporation. It also contains 0.01 per cent of phenyl-alpha-naphthylamine to inhibit oxidation. It is a volatile, clear, practically colourless fluid, showing a slight purplish fluorescence. The specific gravity is 0.77. The boiling point is 28.3–30.6° C. The oil–water solubility varies with the concentration. At anæsthetic con-

centrations it is 41.3. The solubility in water at 37°C. is 5.25 g./100 ml.

Because it is so volatile and so readily oxidized, commercial Vinesthene is issued in sealed dark bottles in small quantities. It should be stored in a cool dark place and kept tightly stoppered. The makers recommend that once a bottle is opened it should be discarded within 24 hours, and that no bottle should be used more than 2 years after the date of issue. Adriani (1941), however, states that bottles, if re-stoppered and kept cool, may be used as long as 10 days after opening, and unopened bottles may be used up to 3 years after issue.

Vinesthene is inflammable and explosive to about the same degree as ethyl ether. It has a characteristically unpleasant smell which may be partially disguised with oil of lavender, eau-de-Cologne, or oil of orange, if so desired.

PHARMACOLOGY

The pharmacology of vinyl ether has been mainly investigated in animals, especially dogs, and the investigation of the clinical effect of the drug is rather incomplete. A survey of the experimental results will therefore precede the description of the clinical effects of the drug.

Experimental Work

The effect of vinyl ether on the central nervous system is typical of the methane series of general anæsthetics. There is a progressive depressant effect, first on the cortex and then on progressively lower levels. Aberrant twitches, sometimes developing into running movements, occasionally occurred during moderately deep anæsthesia in dogs (Goldschmidt et al., 1934). They were generally prevented by morphine-

scopolamine premedication, and the cause was obscure. Vinyl ether was found to have no cholinergic effect, and the only adrenergic effect shown was relaxation of the bronchial musculature (Stevens and Rovenstine, 1941).

Vinyl ether appears in general to have no effect on the heart, and cardiac automaticity, tested with injections of vasopressor drugs, showed no change under vinyl ether anæsthesia (Orth et al., 1940). Some authorities report (Goldschmidt et al., 1934) cases of sudden cardiac arrest in dogs under vinyl ether, but these may have been due to overdose. There is a progressive drop in blood-pressure with deepening anæsthesia.

Vinyl ether is non-irritating to the respiratory tract and, as mentioned before, will relax bronchospasm. It produces salivation in the dog but not in the monkey. Opinions about the action of vinyl ether on the gastro-intestinal tract seem to differ. Experiments *in vitro* showed inhibition of intestinal action (Stevens and Rovenstine, 1941) and a rise in gastric tonus (Orth et al., 1940); but radiological studies in the intact animal (Stevens and Rovenstine, 1941) showed remarkably little disturbance.

The repeated administration of vinyl ether has been shown to produce central zonal necrosis of the liver in dogs (Orth et al., 1940) and this effect could be produced routinely and appeared to be independent of anoxaemia (Goldschmidt et al., 1934). This necrosis, however, did not appear in monkeys. Other workers (Bourne and Raginsky, 1935), using the bromsulphalein test, have, however, found no impairment of liver function, and vinyl ether has no significant effect on bile secretion (Molitor and Kuna, 1941).

Repeated vinyl ether anæsthesias were also shown to produce renal damage in some cases (Leake et al., 1933; Orth

et al., 1940), although no change was observed after a single anæsthesia.

Vinyl ether is absorbed through the lungs like any other anæsthetic vapour (Leake et al., 1933). Most of it is excreted unchanged by the same route. A small quantity is excreted through the kidneys. The initial rate of elimination is very rapid, corresponding to a rapid return to consciousness (Stevens and Rovenstine, 1941). The remainder tends to stay in the fat depots. During light anæsthesia, the oxygen uptake is increased, though in deep anæsthesia, the value decreases to that for normal sleep. Prolonged light anæsthesia without premedication will produce ketonæmia and some hyperglycæmia in rats and rabbits (Leake et al., 1933).

Vinyl ether has been found to be four times more potent than ether (Goldschmidt et al., 1934; Leake et al., 1933). On the other hand, the dose for respiratory arrest is 68 mg./100 ml. against 155 mg./100 ml. for ether. This smaller margin of safety is offset by the fact that, though the extreme volatility of vinyl ether makes it easy inadvertently to give an overdose, resuscitation is relatively easy owing to rapid elimination, combined with the persistence of the heartbeat for some time after respiration has stopped (Draper and Whitehead, 1940).

Clinically vinyl ether resembles other anæsthetics of the methane series in its action on the central nervous system. Occasional twitchings may occur during induction, and convulsions have been reported both during and after operation.

There is no direct effect on the heart although, as might be expected, there is a drop in blood-pressure in deep anæsthesia.

Respiration under vinyl ether is rapid and shallow. It is non-irritant to the respiratory tract (Ogus, 1941) though salivation may occur, especially in unpremedicated patients. Masseter spasm has also been reported. The stomach may have a prolonged emptying time, but clinically the absence of emesis during both induction and recovery is remarkable.

Available liver-function tests (Bourne, 1937a, 1937b) have shown no deleterious effect on the liver during vinyl ether anæsthesia, but cases of liver necrosis following repeated anæsthesias have been reported (Goldschmidt et al., 1934). Mild hyperglycæmia has also been observed on recovery (Stevens and Rovenstine, 1941).

No clinical data is available on renal efficiency during vinyl ether anæsthesia, but one case of hepato-renal syndrome following vinyl ether anæsthesia has been reported (Hawk et al., 1941).

SIGNS OF ANAESTHESIA

The signs of anæsthesia with vinyl ether closely resemble those seen with ether. Induction is rapid with little struggling or excitement. Surgical anæsthesia (Goldsmidt et al., 1934) may be maintained in a light plane, with roving eyeballs but good abdominal relaxation and persisting intercostal movement. Respiration is rapid and shallow in light anæsthesia, but in the third plane of the third stage it becomes jerky with a pronounced expiratory pause, and this is a danger signal which should not be ignored. The eye signs are unreliable, and differ from those seen under ether anæsthesia. On eliciting the eyelid reflex (Ogus, 1941) the eye *opens*. The roving eyeball may persist into the third plane, but usually the eyes are fixed, and the lids relaxed about the middle of the second plane. The pupils dilate in deep anæsthesia.

ANAESTHETIC COMPLICATIONS

Vinyl ether anæsthesia is remarkably free of the usual post-operative complications of nausea and vomiting, and irritation of the respiratory tract. However, two grave complications may occur. Convulsions have been reported both during and after vinyl ether anæsthesia on many occasions (Boston, 1940; Dawkins, 1940; Guerrier and Dafoe, 1940; Durrens, 1941; Kemp, 1944; Smith, 1944; Williams and Sweet, 1944). They appear to be associated with closed methods of anæsthesia—either carbon dioxide absorption, or closed vinyl ether inhalers using a single-dose technique. No cases were reported following the open drop method, and none of the reported cases was fatal.

As already stated, deaths due to central lobular necrosis of the liver (Goldschmidt et al., 1934) have been reported following vinyl ether anæsthesia, and there is a report of one non-fatal case of a hepato-renal syndrome (Hawk et al., 1941).

CLINICAL APPLICATIONS OF VINYL ETHER

Vinyl ether is used in a wide variety of cases, and may be given to patients in any age group (Beach, 1938). Its chief value, however, appears to be in pædiatric anæsthesia, either as the sole agent for short procedures or as an induction agent before the use of ether (Slate, 1942).

It is deservedly popular for dental and oral surgery generally, both alone and in conjunction with nitrous oxide, owing to its potency and great flexibility (Cartin, 1939; Chilton, 1944; Daplyn, 1946; Feldman and Cartin, 1938; French et al., 1940; Seeman, 1940; Wellman et al., 1943; Whitehead and Carter, 1940). A number of workers (Bourne, 1934; Bourne et al., 1937; Bourne, 1937a, 1937b;

Stevens and Rovenstine, 1941; Hartman, 1941; Moffith, 1941) have found vinyl ether very useful in obstetric analgesia and anæsthesia, owing to its potency, its flexibility, and its relative absence of emetic properties.

It has also been used with advantage in war surgery (Rothwell, 1940; Stewart, 1941; Ogus, 1941), owing to its portability and the rapid and complete recovery shown by patients following anæsthesia. These properties also make vinyl ether extremely useful for minor surgery in ambulant patients.

INDICATIONS AND CONTRA-INDICATIONS

Vinyl ether is indicated in any case requiring a potent and flexible anæsthetic agent, where a minimum of apparatus is available. It is also very useful as an induction agent preceding ether. The onset of anæsthesia is rapid and relatively pleasant, and a smoother change-over is generally obtained.

It is contra-indicated in anæsthesia expected to last more than 30 minutes, and in cases (such as versions) requiring deep anæsthesia. It is also contra-indicated in patients with renal or hepatic damage, diabetes, extensive lung disease, or cyanosis. It not the agent of choice in cases of intestinal obstruction or paralytic ileus, or in advanced debility; and it is inadvisable to give it in situations where flame or sparks may be present. If vinyl ether is administered to toxic children, closed methods of anæsthesia are unwise owing to the danger of convulsions.

TECHNIQUES AND APPARATUS FOR ADMINISTRATION

Vinyl ether may be given in a variety of ways. The open drop (Odén, 1942), semi-closed, the closed inhaler (Gold-

man, 1936), and the carbon dioxide absorption techniques have all been used. The open drop method is popular on the American continent, and the closed (single dose) inhaler is much used in Britain, especially for short procedures. Vinyl ether may also be given as part of a balanced anæsthesia with other agents (Brown, 1944; Haley, 1945), and an insufflation technique has also been described using a Junkers bottle (Talleur, 1942).

Vinyl ether–Ether Mixture

Bourne and his co-workers in 1937 suggested the use of a mixture of 25 per cent vinyl ether and 75 per cent ether, in cases requiring longer anæsthesia. They state that induction with this mixture is simple, maintenance is smooth, and the danger of liver damage is minimal. The mixture is much less irritating to the respiratory tract than pure ether.

Vaporization does not materially change the proportions of the mixture (Major, 1937), and Molitor (1937) found that the mixtures producing the most marked shortening of the induction time contained 10 to 30 per cent vinyl ether.

Both Bourne (1934, 1937a, 1937b) and Elam (1939, 1940) recommend the use of this mixture in obstetrics; and other workers have found it valuable in cranial, orthopædic, ear, nose, and throat surgery, as well as lower abdominal surgery.

It may be given by the open-drop technique, or in a closed or semi-closed system. It is less irritating and more potent than pure ether. Recovery is rapid with a minimum of nausea and vomiting. There have been no cases of liver damage reported following the use of vinyl ether–ether mixtures.

SUMMARY

Vinyl ether is a potent and useful anæsthetic agent. It is valuable as an induction agent—especially in pædiatric anæsthesia—and as sole agent in dental anæsthesia, and for other short procedures on ambulant patients.

It is portable, simple to give, and does not involve the use of expensive apparatus. Induction and recovery are rapid and relatively pleasant. It is non-irritating, and resuscitation from overdose is relatively easy.

On the other hand, vinyl ether is very volatile and decomposes rapidly, and is therefore rather uneconomic to use. Its extreme volatility and potency also make it difficult to maintain even anæsthesia. Salivation may be troublesome, and there is the ever-present danger of convulsions and of liver damage after prolonged administration, or repeated small doses. However, in skilled and careful hands, vinyl ether is a valuable agent which could probably be employed with advantage more often than it is today.

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FROM THE MORBIDITY CONFERENCE

ASPIRATION OF VOMITUS

A PRIMIGRAVIDA aged 23 was admitted to hospital at 12.30 p.m. having been in labour $10\frac{1}{2}$ hours. At 10 p.m., after being in the second stage of labour for 2 hours and little advance being made, it was decided to effect a forceps delivery. Premedication of 1/100 grain (0.65 mg.) atropine had been given at 9 p.m. No food had been taken by mouth for 7 hours. The last meal had consisted of tea and bread-and-butter at 3 p.m.

The induction was with gas and oxygen, going on to gas-oxygen–ether. There was no struggling or coughing during induction or during the maintenance of anæsthesia. An episiotomy had been done and while this was being repaired the anæsthesia lightened and the patient vomited. The mask was removed and the mouth opened with a gag and mopped out. The patient became cyanosed. Vomit was aspirated from the throat by suction and the head and shoulders lowered. An endotracheal tube was passed easily and the trachea was aspirated, but little material was obtained. Meanwhile 2 ml. of Coramine was given intravenously. Artificial respiration was instituted but the patient's condition worsened and she died within 2 minutes.

The postmortem examination showed that much food of a broth-like constituency had been aspirated into the small bronchi. The lungs were congested. All other systems were normal.

WRONG INJECTION

In two cases an intravenous injection of adrenaline was given in mistake for atropine at the end of operation. The first case was detected by sudden hæmorrhage from the perineal end of an abdomino-perineal excision of rectum, and the second by an excessive rise in pulse rate. In both instances the atropine and adrenaline ampoules were similar in colour and in the labelling. Fortunately there were no untoward sequelæ in either case.

In another case anæsthesia for a neurosurgical procedure was induced with thiopentone, and 2 ml. of 5 per cent solution left in a 2-ml. syringe in the anæsthetic room should it be required. The anæsthetic room was used by two theatres and a nurse removed the syringes for boiling, the 2-ml. one subsequently being filled with ephedrine for a subject about to have a spinal anæsthetic. 0.5 ml. of this was given to the neurosurgical case in error. Apart from tachycardia, a transient rise in blood-pressure, and undue bleeding there were no ill effects.

PATIENT UNDERGOING TREATMENT WITH HYPOTENSIVE DRUGS

An urgent call was received for an anæsthetist to go to a nearby hospital to anæsthetize a patient for trigeminal neurectomy. The surgeon was waiting and the patient, a woman aged 68, already in the theatre. The case sheet showed that the patient's general condition was 'fair'. There was marked hypertension, blood-pressure 255/120, with the heart generally enlarged, and systolic and aortic murmurs were present. The pulse was regular in rate, force and rhythm. A history of dyspnoea on effort was also present. Respiratory system N.A.D. The patient was edentulous.

A cut-down saline drip was running in the leg and thiopentone 0.6 g. was injected into the drip, the larynx sprayed with 2 per cent amethocaine, and a No. 9 plain orotracheal tube inserted using a Macintosh laryngoscope. Apnoea followed but no bucking. The patient was gently inflated by squeezing the reservoir bag and spontaneous respiration commenced almost immediately. The blood-pressure was checked prior to sitting the patient in the dental chair and was found to be 80 systolic. The pulse was only just palpable at the wrist. On this being reported to the surgeon, the surgical registrar proffered the information that the physicians, in view of the hypertension, had instituted a course of intramuscular hexamethonium, 50 mg. t.d.s. 9 days prior to operation; further, the last 50-mg. dose of hexamethonium had been given half an hour pre-operatively. The patient remained pink, and spontaneous respirations continued. However, on sitting the patient up on the trolley, the systolic blood-pressure fell to 70 after 2–3 minutes and she was returned to the horizontal position. It was noted that the veins of the arms and legs were now dilated. Methedrine 5 mg. was given via the drip and within 4–5 minutes the systolic blood-pressure rose from 70 to 100 mm. Hg and after a further 5 minutes to 120 mm. Hg. The patient was once again sat up and, as the blood-pressure remained at 120/80, the patient was transferred to the dental chair and the operation commenced. The blood-pressure remained at 130/85 throughout the $1\frac{1}{2}$-hour operation. Anæsthesia was maintained by 70 per cent N_2O and 30 per cent O_2 to which was added minimal trichlorethylene using an open Ayres T-piece. Three-quarters of a pint of blood was given during the operation. Hæmorrhage was not excessive, but trouble was experienced from cerebrospinal fluid leaking from a tear of the dura. On comple-

tion of the neurectomy, the retractors were removed and the blood-pressure fell to 90 mm. Hg. This was treated by speeding up the blood-drip, and assumption of the horizontal position. The blood-pressure was 120/80 on leaving the theatre. The postoperative course was uneventful and the patient was discharged on the 24th postoperative day.

Attention is drawn to the potentiation of the hypotensive effect of thiopentone in a patient suffering from hypertension undergoing a course of medical treatment with Vegolysin. Treatment consisted of 5 mg. Methedrine intravenously permitting the operation of trigeminal neurectomy to be performed.

AN AUTOMATIC BREATHING ATTACHMENT TO BOYLE'S APPARATUS

A PRELIMINARY REPORT

By T. M. WILLIAMS

Morriston Hospital, Glamorgan

THE device described has been designed primarily as a small attachment which could be brought quite easily into the circuit of any standard Boyle's machine, thereby making the machine suitable for use as an automatic breathing apparatus in addition to its normal purpose.

The apparatus is actuated by gas pressure alone, and is particularly useful in chest surgery, where respiration may have to be controlled for long periods of time, and also in

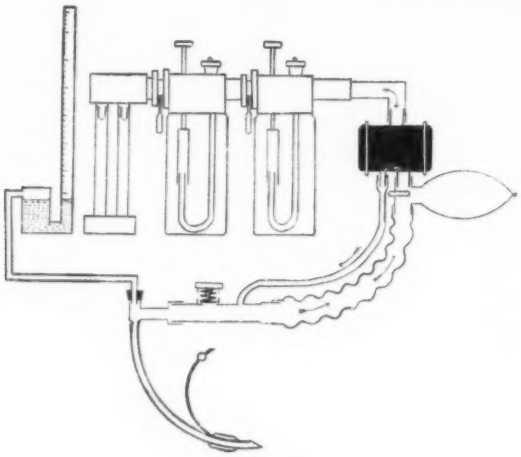


FIG. 2

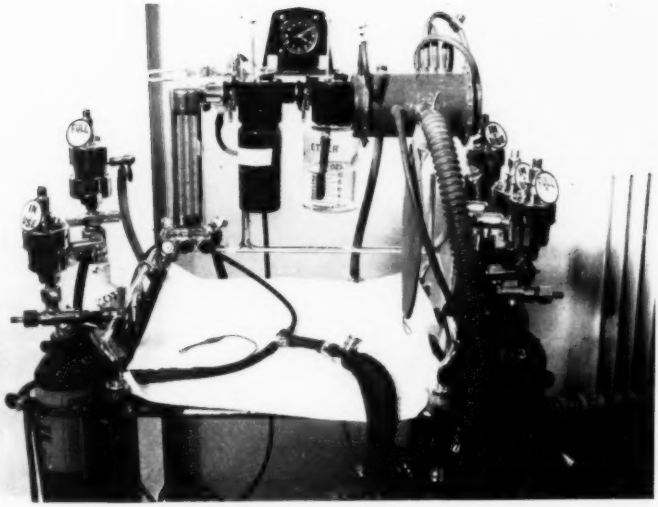


FIG. 1

An automatic breathing attachment to Boyle's machine.

any operation where the attention of the anæsthetist is temporarily diverted elsewhere—such as the setting up of a transfusion—in a patient with inadequate respiratory excursion. It may be used for short or long periods of time, and also in conjunction with Trilene, since no soda-lime is used.

The drawings (figs. 2 and 3) are very slightly modified from those of a home-made prototype which has been in constant use at this hospital for the last 3 years in over 900 major operations.

The apparatus, which can be left as a permanent part of the Boyle's machine, is attached by plugging it in between

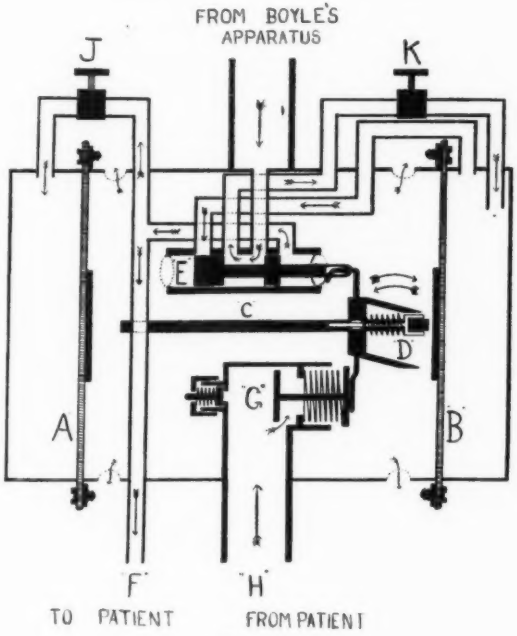


FIG. 3

the last anæsthetic bottle and the bag-mount (fig. 1). The combined machine continues to function as a straightforward Boyle's apparatus for all normal purposes, the usual gas flow passing through the attachment without actuating it. However, should respiration need aiding at any time the apparatus is brought into use merely by closing off the respiratory valve at the face-piece and the re-breathing bag, while at the same time increasing the total gas flow to the maximum the Boyle's machine will give, when the automatic action will commence.

On machines fitted with the Coxeter "bobbin" dry flow meter units, the gases are turned up to 10 litres of oxygen and ten litres of nitrous oxide per minute, but on machines equipped with Rotameter units the necessary flow is obtained by opening to the full both oxygen and nitrous oxide by-pass taps during the automatic action. The attachment is, however, intermittent in type, there being no gas flow during the period of expiration. The consumption of gases is therefore little more than one-half of the above flows. The rate of respiration can be adjusted as desired between 2 and 50 respirations per minute, while intra-pulmonary pressures can be varied at will between $\frac{1}{2}$ and 30 centimetres of water. Considerable variations in both rate and intra-pulmonary pressures are thus possible within these figures.

A water manometer is clipped to the Boyle's machine so that lung pressures can be observed and adjusted during the period of use of the attachment. In order to determine what is the best pressure to use, the patient's lungs are inflated a few times by squeezing the re-breathing bag by hand and noting on the manometer the pressure needed for adequate inflation. The bag is then shut off and the machine set to work at this pressure.

In the case of an adult with a respiratory rate of about 18 per minute and lying on a level table, intra-pulmonary pressures are usually kept below 12 centimetres of water. Should the surgeon wish for a quieter field for a short period of time, as he may do during chest surgery, the lung pressure can be dropped to, say, 5 centimetres of water or less, the rate being kept the same or increased as desired. If a perfectly still but inflated lung is called for, this can be obtained by allowing a suitable leak from the valve at the face-piece (in which case the lung would remain inflated at the pressure behind the leaking valve) or, if preferred, the re-breathing bag can be brought temporarily into the circuit and steady manual pressure exerted on it in the usual way. On closing the expiratory valve and bag-mount the breathing attachment automatically takes over control of respiration once again.

It is found that when spontaneous respiration is returning, an irregular movement of water in the manometer occurs. If it is desired that normal respiration should be resumed the bag-mount and the valve at the face-piece are opened and the gas flows reduced to normal figures. The apparatus then functions once more as a standard Boyle's machine. Very quiet and smooth anæsthesia can be maintained on a mixture of approximately 50 per cent gas and oxygen with, if necessary, any supplementary agent which may be favoured. The patients remain well oxygenated throughout the operation.

The apparatus consists essentially of two stout rubber diaphragms A and B, which act alternately on a central sliding spindle C (fig. 3). This lateral movement of the spindle disturbs the balance of an eccentric cam D which thus moves instantly from one extreme position to the other. The cam is attached to a gas valve E, which in one phase

allows mixed gases to pass via the narrow rubber tubing F directly to the endotracheal tube or face-mask, while in its other phase the valve completely cuts off the gas supply, and by the same movement complete expiration is permitted by the opening of a large-bore expiratory valve G, built into the apparatus, the expired air passing up the corrugated rubber tube H and escaping by means of vents in the casing of the attachment. The respiratory circuit is thus unidirectional, so that dead-space and carbon dioxide retention are reduced to a minimum. In the prototype, change of rate and depth of respiration are controlled by two screw-clips J and K only. When used as a straightforward Boyle's apparatus the patient breathes along the corrugated tube to the re-breathing bag in the usual way, but fresh gases are admitted near the face-piece.

The machine has been in use for over 3 years and during that time no ill effect attributable to it has been noted; on the contrary the patients have been improved by the adequate and even respiratory exchange maintained whenever respiratory depression occurred.

The prototype is still in daily use, but the designs are now in the hands of Mr. A. Charles King, who is making the apparatus for me, and to whom I am very greatly indebted. I should also like to express my grateful thanks to the Surgical Staff, both past and present, at Morriston Hospital for their kind co-operation, and particularly to Dr. W. W. Mushin, Director of Anæsthetics at Cardiff, for his most helpful criticism, advice and interest.

FIG. 1

Y-SHAPED ADAPTOR FOR INTRAVENOUS THERAPY

By M. E. SAMRAH

Brighton General Hospital

The Y-shaped adaptor with taps at distal ends shown in the illustration (fig. 1) is very useful for intermittent thiopentone, Flaxedil, nitrous oxide–oxygen anæsthesia.

The common stem of the "Y" adaptor is joined to a French's needle left in the vein during the course of operation. The syringe containing thiopentone is joined to one stem and held firmly to the forearm with the aid of the "Third Hand" devised by Magill; the remaining branch is left free with tap closed. Use of a French's needle diminishes the possibility of a blockage formed by a blood clot during anæsthesia.

Intravenous injections of d-tubocurarine chloride, Flaxedil, blood, saline or plasma transfusions may be given as necessary through the free stem by adjusting the tap accordingly. The above adaptor saves disconnecting the thiopentone syringe from the needle or using another vein for added intravenous injection during operation.

THE SCOTTISH SOCIETY OF ANÆSTHETISTS

held its annual meeting at Dunblane Hotel Hydro, Perthshire, from Friday, April 25, till Sunday, April 27, 1952. A company of 120—members, their wives and guests—was present.

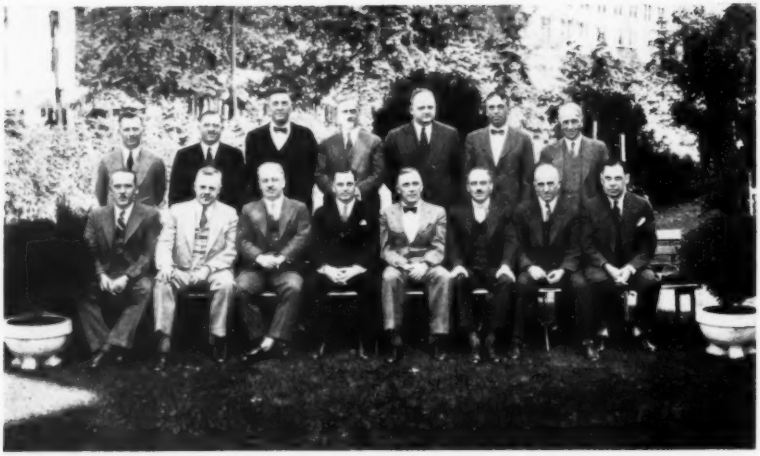
The Executive Council for 1952/53 is as follows:

President: Dr. T. J. C. MacDonald, Aberdeen.
Vice-President: Dr. W. M. Shearer, Dundee.
Hon. Secretary: Dr. R. N. Sinclair, Glasgow.
Dr. H. H. Pinkerton (Glasgow).
Dr. J. D. Robertson (Edinburgh).
Dr. H. W. C. Griffiths (Edinburgh).
Dr. A. G. Miller (Glasgow).
Dr. A. Tindal (Glasgow).
Dr. J. W. L. Bain (Aberdeen).
Dr. M. Muir (Dundee).

The President's Address was in the nature of a pharmacological excursion with the aliphatic halogens having anæsthetic possibilities. Iso-propyl chloride holds out some promise as an analgesic, and experimental work at present proceeding indicates that the fluoro-compounded halogens merit further study.

Dr. M. H. Armstrong Davison, Newcastle, was a guest of the Society, and spoke on the historical background and superstitions surrounding the Mandrake.

The prize which the Scottish Society of Anæsthetists is awarding annually for the best paper submitted from a Registrar was won by Dr. J. P. Payne, Edinburgh.



ANESTHETISTS TRAVEL CLUB

Rochester, Minn., Oct. 2, 1933

Standing, left to right: R. M. Tovell, H. R. Griffith, A. E. Guedel, H. J. Shields, P. M. Wood, P. D. Woodbridge, T. D. Buchanan.

Seated, left to right: H. S. Ruth, W. E. Brown, B. C. Sword, J. S. Lundy, R. M. Waters, C. H. Robson, J. A. Blezard, R. B. Hammond.